

Amendments to the Specification

Please replace paragraph 7 on Page 3 with the following amended paragraph:

[0007] Another process for identifying an analyte molecule involves semiconductor nanocrystals, or quantum dots. Quantum dots can be incorporated into polymeric microbeads at precisely controlled ratios. Each dot has a characteristic spectral emission that can be tuned to a desired energy by varying the particle size, size distribution, and/or composition of the particle. The characteristic emission spectrum can be observed spectroscopically. A drawback with this technique is that it is challenging to incorporate quantum dots into plastic microbeads in a reproducible manner. Although quantum dots do not require multiple lasers and they have narrower emission spectra than dyes, they are difficult to manufacture with reproducible optical properties (both in color and quantum efficiency) and to formulate into solvent-compatible suspensions for embedding into plastic microbeads. Also, they are not generally available in the marketplace, and they are expensive. It would be more desirable to encode microbeads with low-cost methods and with existing materials in the marketplace.

Please replace paragraph 11 on Page 4 with the following amended paragraph:

[0011] Microbeads that are encoded in multiple dimensions present ~~an~~ a virtually unlimited number of identifiers without substantially increasing system processing time. Encoded microbeads that are etched or lithographically divided and separated into a plurality of microbeads can be read in a number of ways, including by means of a specialized reader. The promise of these microbeads could be fulfilled by increasing the speed and accuracy at which they are read.

Please replace paragraph 12 on Page 5 with the following amended paragraph:

[0012] The problems set forth above as well as further and other problems are resolved by the present invention. The solutions and advantages of the present invention are achieved by the illustrative embodiment described herein below. The present invention ~~is~~ is

built on the technology described in United States Patent Application 10/072,837, entitled METHODS FOR MAKING MICROBAR ENCODERS FOR BIOPROBES, incorporated herein in its entirety by ~~reference~~, and reference.

Please replace paragraph 23 on Page 7 with the following amended paragraph:

[0023] FIGs. ~~2M-2S~~ 2M-2N and 2P-2S illustrate, schematically, the microbead formulation of a second alternate embodiment of the present invention in which soft polymeric material is imprinted with a two-level pattern;

Please replace paragraph 24 on Page 7 with the following amended paragraph:

[0024] FIGs. 2T-2W illustrate, schematically, the microbead formulation of a third alternate embodiment of the present invention in which laser ablation ~~in~~ is used to inscribe polymeric material;

Please replace paragraph 29 on Page 8 with the following amended paragraph:

[0029] FIGs. 4A-4~~C~~ 4B schematically illustrate another microbead formulation that is within the illustrative embodiment of the present invention;

Please replace paragraph 48 on Page 16 with the following amended paragraph:

[0048] Referring now to FIGs. ~~2M-2S~~, 2M-2N and 2P-2S, an intermediate embodiment, similar to SFIL, between casting the polymeric material 17 on a patterned master substrate 11 (FIGs. 2A-2F) and embossing polymeric material 17 (FIG. 2G-2L) can be achieved by coating a support substrate 12 with a soft moldable polymeric material 23 and then imprinting a two-level depth patterned master substrate 11, shown in FIG. 2M, against the composite of the support substrate 12 and the soft moldable polymeric material 23, shown in FIG. 2N. Referring to FIG. 2M, the two-level pattern can include a first shallow pattern 27 that forms the perimeter of the microbeads 21 and a second deep relief pattern 28 that forms the encoding of the microbead 21. Two levels are shown herein for illustrative

purposes only, the invention is not limited to two levels of depth. Shown in FIG. 2P, the polymeric material 17 can become cross-linked by heat or light and the imprint can become permanent. The master substrate 11 can be removed, shown in FIG. 2Q, leaving a plurality of supported microbeads 14 on the support substrate 12, shown in FIG. 2R. Finally, in FIG. 2S, microbeads 21 may be freed from the support substrate 12 by use of a release layer (not shown).

Please replace paragraph 51 on Page 17 with the following amended paragraph:

[0051] Referring now to FIG. 2X, a protective layer 53, which can optionally be laid on top of a transducing (e.g. reflective) layer 55, is shown. It is also possible that digital data layer 57, alone, can act as a transducing layer. Alternatively, digital data layer 57 may contain photo-sensitive dyes that can be burned or photobleached with a laser. A transducing system may be formed when digital data layer 57, physically marked in a desired pattern to reveal (or block) a reflective, photoluminescent or absorbing pattern, either may cooperate with transducing layer 55 or may act as a transducing layer itself. Preferably, the transducing system, possibly including transducing layer 55 and/or digital data layer 57 can produce a detectable response signal when exposed to energy. Preferably, the detectable signal produced by the transducing system can be read by an optical reader as binary data. Suitable materials for transducing layer 55 can include films containing silver, indium, antimony, and tellurium. Alternatively, digital data layer 57 may be coated with photo-sensitive dye that may be burned with a laser according to the desired pattern of 1's and 0's (reference # 63), shown as pits 61. Darker and lighter areas, when read, may be understood as binary data. Still further alternatively, phase change technology, involving laser-heating the alloy to two different temperatures, can produce two different crystalline structures. A third laser temperature can be used to read the binary data from the alloy. Using this technology, data may be written more than once, in fact up to 1000 times. Data may be stored more densely by several conventional methods. For example, data may be stored more densely using well-known methods such as Fluorescent Multilayer Optical Data Storage devices (see for example, but not limited to, published United States Patent Application 2002/0098446, and

United States Patent 6,338,935, both of which are incorporated herein in their entirety by reference). Referring now to FIG. 2Y, as described previously, microbeads may be etched from the larger substrate of polymeric material 17, and may be released as individual microbeads 21, shown in FIG. 2Z.

Please replace paragraph 60 on Page 21 with the following amended paragraph:

[0060] Referring now to FIG. 6, a beam of light 71 is projected at an angle onto microbead 21A and 21B which may be etched, molded, embossed, etc. with variously-spaced gratings. The diffracted light from the beam 71 can form an image on a detector arrays 77A and 77B (such as a 1-d or 2-d CCD detector array) where the image may be recorded in the conventional way. In operation, the spacings d_1 and d_2 may work cooperatively under beam 71 to form a diffracted light image that intersects the CCD detector arrays 77A and 77B located at a distance h (reference # 79) above the substrate, making lines of light of spacings L_1 and L_2 on the plane of the CCD detector arrays 77A and 77B. As shown here, for example, if the CCD detector arrays 77A and 77B are one-dimensional (linear) arrays, the projected light may intersect at two or more points along the array separated by the distances L_1 and L_2 . These variables are related by the Bragg diffraction condition $L_{1/2} \sim \lambda_0 h / d_{1/2}$. The distance h (reference # 79) can be small, for example, several hundred microns, or quite large, several millimeters. A series of lines or spots of light from each microbead could be created by patterning the microbead appropriately. In a single-microbead reading configuration, the emission from dyes or luminescent molecules associated with analytes bound to the microbead can be read through a dichroic filter using a conventional fluorescence imaging system (not shown), and simultaneously the size and spacing of the lines or spots can be read at either the same wavelength of the dye emission or at any another wavelength.